

REMARKS/ARGUMENTS

Claims 1-23 are pending, claims 14-23 having been withdrawn from consideration. By this Amendment, claims 1-13 are amended. Support for the amendments to claims 1-13 can be found, for example, in original claims 1-13. The amendments to claims 1-13 are made solely to improve their clarity. No new matter is added. In view of the foregoing amendments and following remarks, reconsideration and allowance are respectfully requested.

Personal Interview

Applicants appreciate the courtesies extended to Applicants' representative by Examiners Palenik and Woodward during the June 5, 2008 Personal Interview. Applicants' separate record of the substance of the interview is incorporated in the following remarks.

Withdrawn Claims

For the reasons set forth below, Applicants submit that all pending claims presently subject to examination are in condition for allowance. Because the withdrawn claims depend from, and thus recite all features of, allowable claim 1, rejoinder and allowance of the withdrawn claims are respectfully requested.

Objection to the Claims

The Office Action objects to claims 8-13 as including informalities. By this Amendment, claims 8-13 are amended to obviate the objection. Accordingly, reconsideration and withdrawal of the objection are respectfully requested.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Office Action rejects claims 1-13 as indefinite under 35 U.S.C. §112, second paragraph. Applicants respectfully traverse the rejection.

The Office Action asserts that claims 1 and 4 conflict because claim 1 recites that the porous material is not silica and claim 4 recites that the porous material is silica. However, Applicants note that claim 1 does not indicate that the porous material may not be any silica, but rather that the porous material may not be a silica having particular characteristics relating to its pore size and X-ray diffraction spectrum. The composition of claim 1 can plainly include silica that does not have these characteristics and, thus, the recitation in claim 4 that the porous material is silica is not inconsistent with claim 1, from which claim 4 depends.

The Office Action asserts that the phrase "very low water-soluble drug" is indefinite. While Applicants do not necessarily agree, claim 1 is amended to specify that "the very low water-soluble drug has a solubility in water at 25 °C of less than 10 µg/mL prior to treatment."

For the foregoing reasons, claims 1-13 are definite. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection Under 35 U.S.C. §102

A. Ohkuchi

The Office Action rejects claims 1-13 under 35 U.S.C. §102(b) over U.S. Patent No. 6,348,468 to Ohkuchi et al. ("Ohkuchi"). Applicants respectfully traverse the rejection.

Claim 1 recites "[a] composition, comprising: a very low water-soluble drug; and a porous material; wherein: the composition is produced by treating a mixture comprising the very low water-soluble drug and the porous material with a supercritical or subcritical carbon

dioxide fluid; the very low water-soluble drug has a solubility in water at 25 °C of less than 10 µg/mL prior to treatment; the porous material is not a porous silica material having an average pore diameter of 1 to 20 nm, where a total pore volume of pores having a diameter falling within a range of  $\pm 40\%$  of the average pore diameter accounts for 60% or more of a volume of all of the pores of the porous material, and having an X-ray diffraction spectrum including one or more peaks at a diffraction angle ( $2\theta$ ) corresponding to  $d$  of 1 nm or more" (emphasis added). Ohkuchi does not disclose or suggest such a composition.

As indicated above, claim 1 requires that the composition be obtained by treating a mixture comprising the very low water-soluble drug and the porous material with a supercritical or subcritical carbon dioxide fluid. The Office Action asserts that Ohkuchi discloses a composition including 5-(4-chlorophenyl)-6-[4-(methylthio)phenyl]-2-benzyl-2H-pyridazin-3-one, corresponding to the very low water-soluble drug of claim 1. *See* Office Action, page 5. The Office Action asserts that the product-by-process step of claim 1, emphasized above, should not be given patentable weight. *See* Office Action, page 4.

At the outset, Applicants note that claim 1 expressly recites a porous material, which is neither disclosed nor suggested by Ohkuchi. Also, while the patentability of a product does not depend on its method of production, the structure implied by process steps should be considered when assessing patentability. *See* MPEP §2114. In this case, Applicants have demonstrated that treating a mixture comprising a very low water-soluble drug and a porous material with a supercritical or subcritical carbon dioxide fluid greatly improves the solubility of the very low water-soluble drug. *See, e.g.*, present specification, page 22, Table 1 (compare Examples 1 to 7 and Comparative Examples 1 and 2). As the composition of claim 1 has different properties than compositions such as in Ohkuchi, the compositions of Ohkuchi cannot be said to anticipate or render obvious the composition of claim 1.

As explained, claim 1 is not anticipated by Ohkuchi. Claims 2-13 depend from claim 1 and, thus, also are not anticipated by Ohkuchi. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

B. Yamamoto

The Office Action rejects claims 1-13 under 35 U.S.C. §102(b) over U.S. Patent No. 5,236,906 to Yamamoto et al. ("Yamamoto"). Applicants respectfully traverse the rejection.

Claim 1 is set forth above. Yamamoto does not disclose or suggest such a composition.

As indicated above, claim 1 requires that the composition be obtained by treating a mixture comprising a very low water-soluble drug and a porous material with a supercritical or subcritical carbon dioxide fluid. The Office Action asserts that Yamamoto discloses a composition including prednisolone valerate acetate. *See* Office Action, page 6. Claim 1 expressly recites a porous material, which is neither disclosed nor suggested by Yamamoto. Also, while the patentability of a product does not depend on its method of production, the structure implied by process steps should be considered when assessing patentability. In this case, Applicants have demonstrated that treating a mixture comprising a very low water-soluble drug and a porous material with a supercritical or subcritical carbon dioxide fluid greatly improves the solubility of the very low water-soluble drug. *See, e.g.*, present specification, page 22, Table 1 (compare Example 8 and Comparative Examples 3 and 4). As the composition of claim 1 has different properties than compositions such as in Yamamoto, the compositions of Yamamoto cannot be said to anticipate or render obvious the composition of claim 1.

As explained, claim 1 is not anticipated by Yamamoto. Claims 2-13 depend from claim 1 and, thus, also are not anticipated by Yamamoto. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection Under 35 U.S.C. §103

A. Nakanishi and Koishi

The Office Action rejects claims 1-11 and 13 under 35 U.S.C. §103(a) over JP 2002-345940 to Nakanishi et al. ("Nakanishi") in view of JP 61-227520 to Koishi et al. ("Koishi"). Applicants respectfully traverse the rejection.

Claim 1 is set forth above. Nakanishi and Koishi do not disclose or suggest such a composition.

As indicated above, claim 1 requires that the composition be obtained by treating a mixture comprising a very low water-soluble drug and a porous material with a supercritical or subcritical carbon dioxide fluid. None of the cited references discloses a composition including these particular components produced in this particular manner. Nakanishi is directed to a methods of preparing a sustained-release composition. *See* Nakanishi, Abstract. That is, Nakanishi is directed to methods of reducing or delaying the solubility of an active ingredient. There is no disclosure in Nakanishi of preparing a composition including a very low water-soluble drug, as recited in claim 1. Moreover, one of ordinary skill in the art would not have been motivated to modify Nakanishi to include a very low water-soluble drug, because doing so would involve attempting to make an active ingredient already having extremely low solubility even less soluble. Such a modification simply would not make sense. *See, e.g.*, MPEP §2143.01.

Koishi is cited for its alleged disclosure of various porous materials having pores filled with drugs. *See* Office Action, page 8. However, the teachings of Koishi do not overcome

the deficiencies of Nakanishi. Neither reference discloses or suggests treating a mixture comprising a very low water-soluble drug and a porous material with a supercritical or subcritical carbon dioxide fluid.

For the reasons discussed above, a *prima facie* case of obviousness has not been made. However, even if a *prima facie* case were made, such case is rebutted by the results shown in the present specification – "[a] *prima facie* case of obviousness ... is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties." See MPEP §2144.09 (citing *In re Papesch*, 315 F.2d 381 (C.C.P.A. 1963)). The Examples of the present specification demonstrate that compositions, such as recited in claim 1, provide superior dissolution properties relative to known compositions, which are not produced by treating a mixture comprising a very low water-soluble drug and a porous material with a supercritical or subcritical carbon dioxide fluid. See, e.g., present specification, page 22, Table 1. These results are objective evidence of the improvements of the composition of claim 1 over known compositions, and thus these results rebut any suggestion that it would have been obvious to combine the teachings of Nakanishi and Koishi as proposed in the Office Action.

As explained, claim 1 would not have been rendered obvious by Nakanishi and Koishi. Claims 2-11 and 13 depend from claim 1 and, thus, also would not have been rendered obvious by Nakanishi and Koishi. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

B. Ohkuchi and Sigma-Aldrich

The Office Action rejects claims 1-13 under 35 U.S.C. §103(a) over Ohkuchi in view of Sigma-Aldrich Silica Gel Product No. 403653 ("Sigma-Aldrich"). Applicants respectfully traverse the rejection.

Claim 1 is set forth above. Ohkuchi and Sigma-Aldrich do not disclose or suggest such a composition.

For the reasons discussed above, Ohkuchi fails to disclose or suggest the composition of claim 1. Sigma-Aldrich does not remedy the deficiencies of Ohkuchi. Sigma-Aldrich is cited for its alleged disclosure of silica having particular properties. *See* Office Action, pages 8 to 9. However, Sigma-Aldrich, like Ohkuchi, fails to disclose or suggest a composition obtained by treating a mixture comprising a very low water-soluble drug and a porous material with a supercritical or subcritical carbon dioxide fluid. Accordingly the combination of references fails to disclose or suggest each and every feature of claim 1.

As explained, claim 1 would not have been rendered obvious by Ohkuchi and Sigma-Aldrich. Claims 2-13 depend from claim 1 and, thus, also would not have been rendered obvious by Ohkuchi and Sigma-Aldrich. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

#### Double Patenting

The Office Action provisionally rejects claims 1-13 under the judicially created doctrine of obviousness-type double patenting over claims 21-24 of U.S. Patent Application No. 10/554,921. Applicants respectfully traverse the rejection.

Claim 1 of the present application recites that "the porous material is not a porous silica material having an average pore diameter of 1 to 20 nm, where a total pore volume of pores having a diameter falling within a range of  $\pm 40\%$  of the average pore diameter accounts for 60% or more of a volume of all of the pores of the porous material, and having an X-ray diffraction spectrum including one or more peaks at a diffraction angle ( $2\theta$ ) corresponding to d of 1 nm or more" (emphasis added). Claim 21 of the 921 application, by contrast, recites that "the porous silica material has an average pore diameter in a range of

from 1 to 20 nm, where pores having diameters within  $\pm 40\%$  of the average pore size account for at least 60% of a total pore volume of the porous silica material, and the porous silica material has an X-ray diffraction spectrum including at least one peak at a position of diffraction angle ( $2\theta$ ) corresponding to a  $d$  value of at least 1 nm" (emphasis added). The porous materials of the claims of the present application and the porous materials of the claims of the 921 application do not overlap and, thus, the claims of 921 application cannot render obvious the claims of the present application.

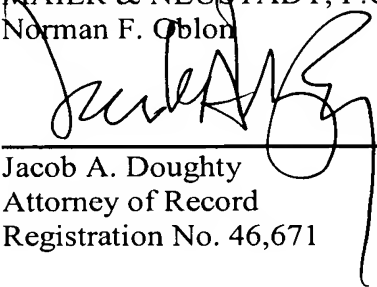
Accordingly, claims 1-13 of the present application are not obvious over claims 21-24 of the 921 application. Reconsideration and withdrawal of the rejection are respectfully requested.

#### Conclusion

For the foregoing reasons, Applicants submit that claims 1-23 are in condition for allowance. Prompt reconsideration and allowance are respectfully requested.

Respectfully submitted,

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